Assessment of the Immunogenicity and Safety of an Unadjuvanted Novartis H1N1 Influenza Vaccine in Special Populations

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Presenter:

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NIAID Influenza Vaccine Clinical Trials in Special Populations

- **Division of Allergy, Immunology and Transplantation**
  - Evaluation of vaccine safety and immunogenicity in severe vs. moderate/mild asthmatics

- **Division of AIDS**
  - Evaluation of vaccine safety and immunogenicity in HIV-infected pregnant women
  - Evaluation of vaccine safety and immunogenicity in perinatally HIV-infected children and adolescents

Assessment of the Immunogenicity and Safety of an Unadjuvanted Novartis H1N1 Influenza Vaccine in Patients with Asthma

- A **randomized phase II clinical trial** to assess the safety and efficacy of an unadjuvanted Novartis H1N1 2009 (S-OIV) influenza vaccine in asthmatics

- **Lead PI**: William Busse, MD (University of Wisconsin, Madison WI)

- **6 other sites** (from NHLBI's Severe Asthma Research Program, SARP): Cleveland Clinic (Erzurum), Wake Forest Univ. (Bleeker), Univ. of Pittsburg (Wenzel), Washington Univ. (Castro), Emory Univ. (Fitzpatrick), and Univ. of Virginia (Gaston/Teague)

Public Health Concerns & Questions

- Patients with asthma appear to be disproportionately represented in H1N1-related deaths in the U.S.; this group should be considered priority for H1N1 immunization; thus, the effectiveness of the H1N1 vaccine needs to be assessed in asthmatics.
- Severe asthmatics receive high doses of inhaled corticosteroids and/or frequent oral steroids; the effects of these agents on vaccine immunogenicity are not known.
- Data is needed quickly on the immunogenicity of H1N1 vaccines in severe asthmatics in order to develop public health policies and recommendations for health care providers (*e.g*. do asthmatics require a higher dose of unadjuvanted vaccine than the general public?).

Objectives - Asthmatics

- **Primary Objectives:**
  - Safety: To assess the safety of the unadjuvanted, inactivated Novartis H1N1 vaccine in asthmatic recipients when administered at the 15 mcg or 30 mcg dose
  - Immunogenicity: To assess the antibody response following a single dose of H1N1 vaccine, stratified by asthma severity of the recipient (mild/moderate vs. severe), when administered twice at either the 15 mcg or 30 mcg dose
- **Secondary Objectives:**
  - Immunogenicity: To assess the antibody response following two doses of H1N1 vaccine, stratified by asthma severity of the recipient (mild/moderate vs. severe), when administered at the 15 mcg or 30 mcg dose

Objectives - Asthmatics

- **Exploratory Objectives:**
  - Safety: New-onset chronic medical conditions through 7 months following the first vaccination
  - Immunogenicity: Immune response as measured by viral neutralization and HA antibody assays following a single dose of vaccine, as well as a second dose given 21 days after the initial dose
  - Development of serum antibody responses against antigenically drifted variants of the novel influenza H1N1 2009 virus
- **Additional Analyses:**
  - Assess the overall effect of age
  - Compare the asthma groups to healthy individuals (from DMID cohorts) with respect to vaccine immunogenicity and safety
  - Immune profiling analysis of banked PBMC RNA in the future

Asthmatics - Study Design

- Enroll 2 groups of asthmatics (about 200 mild/moderate and 150 severe) and randomize 1:1 into 2 vaccine dosing groups levels (15 mcg and 30 mcg per dose x 2 doses).
- Part 1 of this trial will assess short-term safety and the antibody response following vaccination. The two doses of inactivated Novartis influenza H1N1 vaccine will be administered 21days apart.
- Part 2 is a 7 month follow-up to assess long-term safety (new-onset medical conditions and SAEs).

Immunogenicity and Safety in Pregnant Women and in Children/ Adolescents with HIV

- Two separate **phase II clinical trials** to assess the safety and efficacy of 2 doses of 30 mcg unadjuvanted Novartis H1N1 2009 influenza vaccine in pregnant women with HIV
- **Lead PIs**: **Sharon Nachman, MD** (State University of New York at Stony Brook) for pregnant women's study, **Pat Flynn, MD** (St. Jude's Hospital for Children, Memphis, Tennessee) for pediatric study
- **35 domestic study sites** within the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network

Public Health Concerns & Questions

- Pregnant women appear to be disproportionately represented in H1N1-related deaths in the U.S. and elsewhere
- HIV-infected pregnant women and children may at particular risk for increased morbidity of H1N1
- H1N1 vaccines may be less immunogenic in HIV-infected pregnant women and children thus lower doses may not provide adequate protection
- Higher titer vaccines have yielded better immune response in elderly (seasonal flu) and HIV-infected adolescents (HBV)
- Infants born to HIV-infected women are at risk for H1N1 infection and are ineligible for vaccination until 6 months old – antibodies that cross the placenta will provide some protection

Objectives – HIV in Pregnancy

- **Primary Objectives:**
  - To determine the safety and immunogenicity after each of two doses of the Novartis H1N1 2009 vaccine in HIV-1-infected pregnant women.
- **Secondary Objectives:**
  - To assess the maternal level of H1N1 antibody at delivery following administration of two doses of the H1N1 vaccine to HIV-1 infected pregnant women
  - To assess the extent of placental transport H1N1 antibody from mother to the neonate by measuring this antibody in cord blood
  - To assess the persistence in the neonate, of maternal H1N1-specific antibodies at birth and 3 months of age.
  - To evaluate influenza-like illness two weeks after completing study vaccination through clinic visits for all acute febrile and respiratory illnesses, including acquisition of nasal swabs for determination of influenza with RT-PCR.
  - To assess maternal cell-mediated immune responses to the H1N1 vaccine.

Objectives – Pediatric HIV

- **Primary Objectives:**
  - To determine the safety and immunogenicity after each of two doses of the Novartis H1N1 2009 vaccine in HIV-1 perinatally infected children and adolescents.
- **Secondary Objectives:**
  - To correlate vaccine response with baseline antibody titer.
  - To assess persistence of antibody response 6 months after the second dose of the H1N1 vaccine.
  - To correlate immune responses with CD4+ cell count, CD4%**,** ARV use, plasma HIV-1 RNA concentration at the time of first immunization, and with timing of seasonal influenza vaccine.
  - To assess cell-mediated immune responses to the H1N1 vaccine.
  - To describe influenza-like illness (ILI) occurring during the course of the study, plus collection of respiratory specimens for determination of influenza with RT-PCR.

Study Design - HIV

- All subjects will receive 30 mcg per dose x 2 doses
- Pregnant women (130 subjects) will have first vaccination between 14 and 35 weeks gestation, and **both mothers and infants will be assessed through 6 months post-partum**
- Pediatric patients will be stratified into 3 age-based cohorts (40 subjects per age group); although not stratified by CD4 count, data will be analyzed relative to such